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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,466	09/19/2006	Mariusz W. Szkudlinski	TROP-001/01US 304828-2046	9091

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ART UNIT	**PAPER NUMBER**
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,466	SZKUDLINSKI ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-137* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 7-14,16-25,29-39,47-51,53-57,59-66,68-83,94,96,100-103,110,112,116-119,124-126 and 130-135.

Continuation of Disposition of Claims: Claims rejected are 1-6,11,12,15,26-28,40-42, 44-46,52,58,67,84-93,95,97-99,104-109,111,113-115,120-123,127-129,136 and 137.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 5 October 2009 is acknowledged. In addition, Applicants elected the modified FSH α-subunit species of Q13R, E14R, P16R and Q20R. Further, Applicants elected the species of additional modification of FSH β chain consisting of E4R. Applicants request the additional examination of claims 7 and 9, 10, 13 and 14, because they assert the claims are encompassed by the species election. This is not found persuasive, as these claims encompass modified FSH superagonists not elected by Applicants. In addition, upon examination of the claims, it was found that claims 102, 103, 118, 119, 132 and 133 are ***not*** among the elected species since they require a basic amino acid substitution at residue 4 of the alpha subunit and the elected species is an FSH superagonist with arginine (R) substitution(s) at residues 13, 14, 16 and 20. Claims 7, 8, 9-14, 16-25, 29-39, 47-51, 53-57, 59-66, 68-83, 94, 96, 100-103, 110, 112, 116-119, 124-126, 130, 131-134 and 135 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5 October 2009.

Claims 1-6, 11, 12, 15, 26-28, 40-46, 52, 58, 67, 84-93, 95, 97-99, 104-109, 111, 113-115, 120-123, 127-129, 136 and 137 are under examination.

Claim Objections

Claims 6 and 42 are objected to because of the following informalities. The standard way to write sequence identifiers is “SEQ ID NO: 1" or “SEQ ID NO: 2”. However, claims 6 and 42 recite "SEQ ID No. X”.

Claims 84, 107 and 108 are objected because of the following informalities. The claims recite “□-subunit”, though presumably “α-subunit” was intended.

Claim 1, is objected to because in line 3 the “a” in the phrase “a ten fold” is awkward grammatically. It is suggested that the claim recite “at least about ten fold”.

Claim 43 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-6, 11, 12, 15, 26-28 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 does not constitute a proper Markush group since it does not end with an "or" or an "and" for the last FSH, but rather it ends with “etc.”, which is not limiting. Claims 5-6, 11, 12, 15, 26-28, 40 are rejected because they depend from indefinite claim 4.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 46 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cultured or isolated host cell comprising the vector of claim 45, wherein the host cell is suitable for expressing the nucleic acid, does not reasonably provide enablement for host cell comprising the vector of claim 45, wherein the host cell is suitable for expressing the nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a broad genus of host cells comprising an expression vector which, in turn, comprises the claimed DNA. The specification contemplates three subgenera in which such host cells can be made and used. Specifically, the specification contemplates making and using the host cells in culture and “in vivo" (see paragraph [0076]), which encompasses gene therapy, and expression in multicellular, transgenic organisms.

Case law directs that the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled. The standard is whether a

skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). However, claims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. *Ibid.*; *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). Since the instant specification asserts that the claimed host cells can be made and used in three contexts, two of which are not enabled for the reasons set forth below, the instant fact pattern corresponds to the second situation wherein the claims encompass a significant number of inoperative embodiments and thus should be rejected under 35 U.S.C. § 112, first paragraph, as not being enabled for the full scope of the claims.

The specification asserts that host cells can be made and used in three contexts. 1) The specification contemplates making and using isolated host cells in culture to produce the encoded protein recombinantly. Such is enabled, since the specification and prior art provide specific guidance on how to make and use isolated host cells for this purpose. Undue experimentation would not have been required of the skilled artisan to make and use the claimed host cells in this context.

2) The specification also asserts that the claimed gene products can be expressed in vivo, which encompasses expression in transgenic animals by techniques

known in the art (again, see paragraph [0076], also [0070]). However, there are no methods or working examples disclosed in the instant application whereby a multicellular animal with the incorporated claimed gene is demonstrated to express the encoded peptide. There are also no methods or working examples in the specification indicating that a multicellular animal has the claimed gene “knocked out”. The unpredictability of the art is *very high* with regards to making transgenic animals. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood. 1999; 94: 3178-3184) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2nd full paragraph; pg 3182-3183). The literature also teaches that the production of transgenic animals by microinjection of embryos suffers from a number of limitations, such as the extremely low frequency of integration events and the random integration of the transgene into the genome which may disrupt or interfere with critical endogenous gene expression (Wigley et al. Reprod Fert Dev. 1994; 6: 585-588).

3) Again, the teaching in the specification that nucleotide constructs comprising the claimed gene can be used to express such products in vivo encompasses gene therapy (see paragraph [0076]). However, the specification does not teach any methods or working examples that indicate the claimed nucleic acid is introduced and

expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the claimed nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express the claimed nucleic acid into the cell of an organism to treat disease. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express the claimed nucleic acid in the cell of an organism or be able to produce the encoded protein in that cell.

Due to the large quantity of experimentation necessary to generate a transgenic animal expressing the disclosed protein and to introduce and express the claimed nucleic acid in a cell of an organism for therapy, the lack of direction/guidance

presented in the specification regarding how to introduce the claimed nucleic acid in the cell of an organism to be able produce the encoded protein, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of making transgenic animals and the unpredictability of transferring genes into an organism's cells, and the breadth of the claims which fail to recite any cell type limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Please note that this rejection could be overcome by amending the claims to recite, for example, “An cultured host cell…” because such an amendment would clarify that the claims are directed only to host cells which are to be made and used in culture as described in context 1) above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 11, 12, 15, 26-28, 40, 44-46, 52, 67, 84-93, 95, 97-99, 104-109, 111, 113-115, 120-123, 127-129, 136 and 137 are rejected under 35 U.S.C. 102(b) as being anticipated by Szkudlinski et al. (WO97/42322, US HEALTH published 13 November 1997) and Szkudlinski et al. (U.S. Patent Publication 2002/0110909, published 15 August 2002). These documents are part of the same family.

The claims are drawn to a modified follicle stimulating hormone or FSH superagonist having increased half-life and activity compared to wild-type FSH and having two or three basic amino acid substitutions selected from the group consisting of positions 13, 14, 16, 17, 20, 21, 22, 66, 68, 73, 74 and 81 the SEQ ID NO: 1 (i.e., the α-subunit of FSH), wherein said basic amino acid is arginine; nucleic acids encoding said superagonists, as well as vectors and host cells suitable for expressing said nucleic acids; methods of treating infertility and improving oocyte quality in animals.

The WO97/42322 document teaches a modified glycoprotein hormone wherein there are three or four basic amino acid substitutions selected from the group consisting of positions 11, 13, 14, 16, 17 and 20 of the α-subunit of FSH (see, for example, pages 3, 6, whole pages; p. 8, lines 19-30; p. 17, lines 6-29; p. 18, lines 1-18; p. 19, lines 5-16; claims 1-11, 18, 22). The WO97/42322 document teaches two to five basic amino acid substitutions selected from the group consisting of amino acids 13, 14, 16, 17 and 20, which falls squarely into the range recited in the claims. First, see MPEP § 2131.03 for case law pertaining to rejections based on the anticipation of ranges under 35 U.S.C. 102.

> I. A SPECIFIC EXAMPLE IN THE PRIOR ART WHICH IS WITHIN A CLAIMED RANGE ANTICIPATES THE RANGE
>
> "[W]hen, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is anticipated' if one of them is in the prior art." Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (citing In re Petering, 301 F.2d 676, 682, 133 USPQ 275, 280 (CCPA 1962)) (emphasis in original) (Claims to titanium (Ti) alloy with 0.6-0.9% nickel (Ni) and 0.2-0.4% molybdenum (Mo) were held anticipated by a graph in a Russian article on Ti-Mo-Ni alloys because the graph contained an actual data point corresponding to a Ti alloy containing 0.25% Mo and 0.75% Ni and this composition was within the claimed range of compositions.).

As noted above, the range taught in WO97/42322 is narrower than and falls squarely within the range recited in the claims. Further, basic substitutions specifically at residues 16 and 20 of the α-subunit are taught at p. 17, line 30 of the WO97/42322 document (claim 11); basic substitutions specifically at residues 13, 14, 16 and 20 are taught at p. 19, line 13 and claims 5 and 18. Basic amino acids are selected from the group lysine, arginine and histidine (see p. 9, line 1; p. 18, line 18; p. 19, lines 16 and 26-27 and claim 22 of the WO97/42322 document). Note that claims 1 and 2 of the WO97/42322 document recite:

1. A human glycoprotein hormone comprising at least three basic amino acids in the α-subunit at positions selected from the group consisting of positions 11, 13, 14, 16, 17, and 20.
2. The human glycoprotein hormone of claim 1, further comprising a fourth basic amino acid at a position selected from the group consisting of positions 11, 13, 14, 16, 17, and 20.

Claim 5 of the WO97/42322 document recites:

The human glycoprotein hormone of claim 2, wherein basic amino acids are at positions 13, 14, 16, and 20.

Further note that claim 18 of the WO97/42322 document recites:

The glycoprotein hormone of any of claims 1 - 11, wherein the hormone is follicle-stimulating hormone.

And finally, that claim 22 of the WO97/42322 document recites:

The human glycoprotein hormone any of claims 1 - 20, wherein the basic amino acids are selected from the group consisting of lysine and arginine.

Thus, the WO97/42322 document clearly teaches an FSH variant with arginine substitutions at residues 13, 14, 16 and 20 of the α-subunit, and meets the claim limitations recited in claims 28, 93, 109 and 123.

The WO97/42322 document teaches modification of the analogs to increase half life, for example at p. 35, lines 22-23. Second, the FSH variants described therein would also have superagonist properties (increased absorption, binding affinity, half-life, positively charged at neutral pH) since the same substitutions are contemplated. See In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963): "[f]rom the standpoint of patent law, a compound and all its properties are inseparable." Since the WO97/42322 document teaches recombinant methods of making proteins, suitable hosts and vectors therefor, the limitations of claims 44-46 are also met. Further, it is taught in the WO97/42322 document that the contemplated modified glycoprotein hormones have increased activity, for example at pages 22 and 23. Finally, the WO97/42322 document also teaches methods of assisted reproduction, for example, at p. 24, lines 25-30 and p. 26, lines 4-12. Injection is contemplated at p. 25, line 20. The method claims in the instant specification recite methods of administering an effective amount of FSH superagonist containing basic amino acid substitutions at one or more positions selected from 13, 14, 16 and 20 to improve the quality of oocytes in a human or an animal (claims 84-92, 95, 97-99); to induce superovulation (claims 104-108, 111, 113-115); to enhance superovulation (claims 120-122, 127-129). Since the same exact superagonist is contemplated for the same exact population (those in need of assisted reproduction), it is inherent to the methods taught in the WO97/42322 document that they would also achieve the same goals as recited in the method claims cited herein.

As noted above, U.S. Patent Publication, 2002/0110909, is a related document and the corresponding citations anticipating the claims are found at claims 1, 2, 5, 18,

25, 27 and 29; paragraphs [0004], [0006], [0031]-[0041]; [0045], [0050], [0051], [0053]-[0055], [0073], [0074].

Claims 1-5, 41-42, 44-46, 52, 58, 67, 136 and 137 are rejected under 35 U.S.C. 102(b) as being anticipated by Schambye et al., (Patent Publication No. 2002/0127652, published 12 September 2002). Claims 1-5 and 44-46 are drawn to FSH superagonists having a modified α-subunit and increased potency, wherein said modified FSH is human (among others) and nucleic acids, vectors encoding them, and host cells for expressing them; claims 41-42 encompass FSH superagonists having additionally at least one basic amino acid substitution selected from the group consisting of residues 2, 4, 14, 63, 64, 67, 69 of SEQ ID NO: 2 (i.e., the β-subunit of FSH). In addition, claims 52 and 58 are drawn to increasing half life and the addition of polyethylene glycol (PEG), respectively.

Schambye et al. teach a modified FSH having the introduction of a basic amino acid (i.e., a lysine residue) in the α-subunit, and also teaches the introduction of a lysine residue into the β-subunit, for example, residues 2, 4, 64, 67, and 69 (see paragraphs [0115]-[0116]), thus meeting the limitations of claims 1 and 41-42. Recombinant methods of protein expression are contemplated at paragraphs [0179]-[0180], including nucleic acids, vectors and host cells, thus meeting the limitations of claims 44-46. In addition, Schambye et al. contemplate human FSH at paragraph [0057]. Because Schambye et al. contemplate the same basic amino acid substitutions as recited in the rejected instant claims, it is inherent that such FSH variants would have the same

properties, such as increased potency, absorption and binding affinity. See In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963): "[f]rom the standpoint of patent law, a compound and all its properties are inseparable." Schambye et al. teach that their FSH variants have increased half-life and discuss the conjugation of PEG to the polypeptides to increase half-life (see, for example, abstract; claim 25; paragraphs [0122]-[0123] and [0137]), thus meeting the limitations of claims 52 and 58). Finally, Schambye et al. contemplate administration of the FSH superagonists for treatment of infertility, thus meeting the limitation of claim 67.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Szkudlinski et al. (WO97/42322, US HEALTH published 13 November 1997) or Szkudlinski et al. (U.S. Patent Publication 2002/0110909, published 15 August 2002) as applied above to claims 1-6, 11, 12, 15, 26-28, 40, 44-46, 52, 67, 84-93, 95, 97-99, 104-109, 111, 113-115, 120-123, 127-129, 136 and 137, above and further in view of Schambye et al., (Patent Publication No. 2002/0127652, published 12 September 2002).

The first issue is to determine the scope and contents of the prior art. The limitations of claims 1-6, 11, 12, 15, 26-28, 40, 44-46, 52, 67, 84-93, 95, 97-99, 104-109, 111, 113-115, 120-123, 127-129, 136 and 137 and how they are met by both of the Szkudlinski documents is discussed above in detail and is hereby incorporated. The second issue is to ascertain the differences between the prior art and the instant claims. Neither of the Szkudlinski documents specifically mention PEGylation of the FSH variants. Schambye et al. teach at paragraph [0137] the addition of PEG in order to increase functional in vivo half-life and/or serum half-life. The level of skill in the prior art is high with respect to PEGylation of polypeptides. Finally, one must consider

objective evidence present in the application indicating obviousness. There is no specific evidence present in the instant application that PEGylation results in any surprising or unexpected results beyond what is taught in the prior art, namely, PEGylation is suitable for reducing immunogenicity and/or increasing functional in vivo half-life and/or serum half-life.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the teachings of Szkudlinski by PEGylating the FSH superagonists, as taught in Schambye et al. because Schambye et al. teach that PEG is suitable for reducing immunogenicity and/or increasing functional in vivo half-life and/or serum half-life. The person of ordinary skill in the art would have been motivated to make the modification because, as taught in Schambye et al., PEGylation results in a need for fewer injections (for instance, see paragraph [0196] of Schambye et al.). Furthermore, the person of ordinary skill in the art could have reasonably expected success because PEGylation is old in the art, and well understood to be effective at reducing immunogenicity and increasing half-life. Thus the claims do not contribute anything non-obvious over the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 11, 12, 15, 26-28, 40, 44-46, 52, 136 and 137 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 of U.S. Patent No. 7,070,788. Although the conflicting claims are not identical, they are not patentably distinct from each other because in both cases, the claims are drawn to modified human FSH having basic amino acid (i.e., lysine or arginine) substitutions at positions 11, 13, 14, 16, 17 and 20, nucleic acids, vectors and host cells for expressing said FSH variants. The difference between the claim sets lies in the fact that the instant claims 1-6, 11, 12, 15, 26-28, 40, 44-46 and 52 do not recite that the modified FSH contains a β-subunit. Further, the claims of the '788 patent do not teach increased potency, absorption or binding affinity, nevertheless, since the '788 patent teaches the same FSH α-subunit modifications, the same polypeptides are claimed, thus it follows that they must also have the same properties.

Claim 58 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 of U.S. Patent No. 7,070,788 in view

of Schambye et al. As noted above, Schambye et al. teach that PEGylation of FSH increases its half-life and reduces immunogenicity. It would be obvious to modify the claimed FSH variants of the '788 patent by conjugating PEG to the polypeptide because doing so would increase the plasma half life.

Conclusion

Claims 1-6, 11, 12, 15, 26-28, 40-42, 44-46, 52, 58, 67, 84-93, 95, 97-99, 104-109, 111, 113-115, 120-123, 127-129, 136 and 137 are rejected. Claim 43 contains allowable subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is (571)272-4482. The examiner can normally be reached on 9:00am - 3:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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